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Dialog level 99.05.27D

Last logoff: 15jul99 12:13:45

Logon file001 27jul99 13:57:30

ANNOUNCEMENT **** ANNOUNCEMENT **** ANNOUNCEMENT

NEW

***Market Guide Company Financials (File 100)

***Frost & Sullivan Market Engineering (File 767)

***Canada Newswire (File 616 for current news, File 816 for archive)

***So America Bus Info (File 617 for current news, File 817
for archive news)

***UPI News (Files 261 for current news & 861 for archive news)

***Africa News (Files 606 for current news & 806 for archive news)

***ITAR/TASS (Files 607 for current news & 667 for archive news)

***Xinhua News (Files 618 for current news & 818 for archive news)

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***PR Newswire (Files 613 for current news & 813 for archive news)

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***Aerospace/Defense Markets & Technology (File 80)

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>>> of new databases, price changes, etc. <<<

File 1:ERIC 1966-1999/Jul

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Set Items Description

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? b 410

>>>'IALOG' not recognized as set or accession number

? set hi ;set hi

27jul99 13:57:37 User208709 Session D447.1

\$0.26 0.080 DialUnits File1

\$0.26 Estimated cost File1

FTSNET 0.016 Hrs.

\$0.26 Estimated cost this search

\$0.26 Estimated total session cost 0.080 DialUnits

File 410:Chronolog(R) 1981-1999 Jul/Aug
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? b 155

27jul99 13:58:00	User208709	Session D447.2
\$0.00	0.041	DialUnits File410
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File 155:MEDLINE(R) 1966-1999/Sep W3
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*File 155: reloaded, note accession numbers changed.

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? s intestinal(w)transcytosis

168624	INTESTINAL
481	TRANSCYTOSIS
S1	2 INTESTINAL(W)TRANSCYTOSIS

? t s1/7/1-2

1/7/1

DIALOG(R) File 155:MEDLINE(R)
(c) format only 1999 Dialog Corporation. All rts. reserv.

09152238 97308306

Enhanced oral uptake of tomato lectin-conjugated nanoparticles in the rat.

Hussain N; Jani PU; Florence AT
Centre for Drug Delivery Research, School of Pharmacy, University of London, United Kingdom.

Pharm Res (UNITED STATES) May 1997, 14 (5) p613-8, ISSN 0724-8741
Journal Code: PHS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

PURPOSE: To investigate the usefulness of a surface-conjugated, bioadhesive molecule, tomato lectin, to augment intestinal uptake of orally administered inert nanoparticles. METHODS: Fluorescent 500 nm polystyrene nanoparticles with tomato lectin covalently surface coupled using a carbodiimide reaction were administered to female Wistar rats by oral gavage daily for 5 days. RESULTS: Analysis of tissue extracted polymer by gel permeation chromatography revealed a 23% systemic uptake of tomato lectin conjugated nanoparticles compared to < 0.5% of TL nanoparticles blocked with N-acetylchitotetraose thus representing an increase of almost 50 fold across the intestine. Intestinal uptake of tomato lectin-conjugated nanoparticles via the villous tissue was 15 times higher than uptake by the gut-associated lymphoid tissue. CONCLUSIONS: The application of tomato lectin as a bioadhesive agent in vivo has been demonstrated to enhance subsequent **intestinal transcytosis** of colloidal particulates to

which it is bound.

1/7/2

DIALOG(R)File 155:MEDLINE(R)

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08671265 96182303

Abnormally short serum half-lives of IgG in beta 2-microglobulin-deficient mice.

Ghetie V; Hubbard JG; Kim JK; Tsen MF; Lee Y; Ward ES

Department of Microbiology, University of Texas Southwestern Medical Center, Dallas 75235-8576, USA.

Eur J Immunol (GERMANY) Mar 1996, 26 (3) p690-6, ISSN 0014-2980

Journal Code: EN5

Contract/Grant No.: AI32413, AI, NIAID; AI33111, AI, NIAID

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The MHC class I-related receptor, FcRn, mediates the transfer of maternal gamma globulin (IgG) to young rodents, primarily via **intestinal transcytosis**, and this provides humoral immunity for the first few weeks after birth. In a previous study, the site of mouse IgG1 (mIgG1) with which FcRn interacts has been mapped using recombinant wild-type and mutated Fc-hinge fragments. The site encompasses residues at the CH2-CH3 domain interface of Fc (Ile253, His310, Gln311, His433 and Asn434) and the same amino acids are involved in regulating the pharmacokinetics of the Fc-hinge fragments. This suggests that in addition to its known function, FcRn might also play a role in IgG homeostasis. Consistent with this hypothesis, in this study, we demonstrate that FcRn alpha-chain mRNA is present not only in neonatal brush border but also in other tissues of adult animals (liver, lung, spleen and endothelial cells). In addition, analysis of the pharmacokinetics of mouse Ig/Fc-hinge fragments in genetically manipulated mice that are deficient in the expression of FcRn demonstrates that the beta-phase half-lives are abnormally short. These findings suggest that FcRn is involved in IgG homeostasis.

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? s transcytosis and antibod?

481 TRANSCYTOSIS

518407 ANTIBOD?

S2 113 TRANSCYTOSIS AND ANTIBOD?

? s s2 not py>1995

113 S2

1362833 PY>1995

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113 S2

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113 S2

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87749 F

701278 C?

457 F(W)C?

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113 S2
25405 FC?
S6 11 S2 AND FC?
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DIALOG(R)File 155:MEDLINE(R)
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09516515 98236755

Current concepts in mucosal immunity. IV. How epithelial transport of IgA **antibodies** relates to host defense.

Iamm ME
Institute of Pathology, Case Western Reserve University, Cleveland, Ohio 44106, USA.

Am J Physiol (UNITED STATES) Apr 1998, 274 (4 Pt 1) pG614-7, ISSN 0002-9513 Journal Code: 3U8

Contract/Grant No.: AI-26449, AI, NIAID; AI-36359, AI, NIAID

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

The humoral arm of the mucosal immune system is principally composed of locally synthesized polymeric IgA, whose **Fc** portion is adapted for binding to the polymeric immunoglobulin receptor that is expressed on the basolateral surface of mucosal epithelial cells, including enterocytes. This receptor mediates the endocytosis and **transcytosis** of polymeric IgA, which allows IgA to function in host defense at three anatomic levels in relation to mucosal epithelium: IgA **antibodies** in the lamina propria can bind antigens and excrete them through the epithelium into the lumen; antiviral IgA **antibodies** in transit through epithelial cells can inhibit virus production by an intracellular action; and IgA **antibodies** secreted into the lumen can prevent antigens and microbes from adhering to and penetrating the epithelium. The ways in which IgA **antibodies** function in mucous membranes provide challenging investigative opportunities for cell physiologists and cell biologists. (22 Refs.)

6/7/2
DIALOG(R)File 155:MEDLINE(R)
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09489496 98198471

Apical plasma membrane proteins and endolyn-78 travel through a subapical compartment in polarized WIF-B hepatocytes.

Ihrke G; Martin GV; Shanks MR; Schrader M; Schroer TA; Hubbard AL
Department of Cell Biology and Anatomy, The Johns Hopkins School of Medicine, Baltimore, Maryland 21205, USA.

J Cell Biol (UNITED STATES) Apr 6 1998, 141 (1) p115-33, ISSN 0021-9525 Journal Code: HMV

Contract/Grant No.: P01-NIDDK 44375

Languages: ENGLISH

Document type: JOURNAL ARTICLE

We studied basolateral-to-apical **transcytosis** of three classes of apical plasma membrane (PM) proteins in polarized hepatic WIF-B cells and then compared it to the endocytic trafficking of basolaterally recycling membrane proteins. We used **antibodies** to label the basolateral cohort of proteins at the surface of living cells and then followed their trafficking at 37 degreesC by indirect immunofluorescence. The apical PM

proteins aminopeptidase N, 5'nucleotidase, and the polymeric IgA receptor were efficiently transcytosed. Delivery to the apical PM was confirmed by microinjection of secondary **antibodies** into the bile canaliculus-like space and by EM studies. Before acquiring their apical steady-state distribution, the trafficked **antibodies** accumulated in a subapical compartment, which had a unique tubulovesicular appearance by EM. In contrast, **antibodies** to the receptors for asialoglycoproteins and mannose-6-phosphate or to the lysosomal membrane protein, lgp120, distributed to endosomes or lysosomes, respectively, without accumulating in the subapical area. However, the route taken by the endosomal/lysosomal protein endolyn-78 partially resembled the transcytotic pathway, since anti-endolyn-78 **antibodies** were found in a subapical compartment before delivery to lysosomes. Our results suggest that in WIF-B cells, transcytotic molecules pass through a subapical compartment that functions as a second sorting site for a subset of basolaterally endocytosed membrane proteins reaching this compartment.

6/7/3

DIALOG(R)File 155:MEDLINE(R)

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09455917 98154319

Structural basis of pH-dependent **antibody** binding by the neonatal **Fc** receptor.

Vaughn DE; Bjorkman PJ

Division of Biology, California Institute of Technology, Pasadena 91125, USA.

Structure (ENGLAND) Jan 15 1998, 6 (1) p63-73, ISSN 0969-2126

Journal Code: B31

Contract/Grant No.: AI/GM41239, AI, NIAID

Languages: ENGLISH

Document type: JOURNAL ARTICLE

BACKGROUND: The neonatal **Fc** receptor (**FcRn**) mediates the **transcytosis** of maternal immunoglobulin G (IgG) across fetal and/or neonatal tissues for the acquisition of passive immunity. In adults, **FcRn** is involved in the maintenance of high serum IgG levels. Both processes are mediated by pH-dependent IgG binding to **FcRn-FcRn** binds to IgG with nanomolar affinity at pH 6, but shows no detectable binding at pH 7.5. At pH 6, **FcRn** is more thermally stable and the dissociation rate of its light chain is an order of magnitude slower than at pH 8.0. Comparison of the structures of **FcRn** at pH 6.5 and pH 8 allows an analysis of the structural basis for the receptor's pH-dependent ligand binding and stability. RESULTS: We have determined the structure of **FcRn** at pH 8 and compared it to a further refined version of the structure at pH 6.5. An extensive ordered carbohydrate structure is observed at both pH values. The two structures are very similar; thus the pH dependence of **FcRn** stability and affinity for IgG can be attributed to chemical properties of the structures themselves, rather than mechanisms that rely on conformational changes. The pH-dependent properties are mediated by electrostatic interactions involving histidine residues, which are more favorable for the protonated form of histidine that predominates at acidic pH values. CONCLUSIONS: No major conformational change is observed between the pH 6.5 and pH 8 structures of **FcRn** that could account for the differences in affinity for IgG. The pH dependence of IgG binding to **FcRn** can therefore primarily be attributed to titration of histidine residues on **Fc** that interact with anionic pockets on the receptor. The **FcRn** dimer, which is required for high affinity binding of IgG, is itself stabilized at acidic pH by histidine-mediated salt bridges and a sidechain rearrangement that creates a more favorable interaction with an anionic pocket at pH 6.5

relative to pH 8. **FcRn** dimerization is facilitated by reciprocal interactions in which carbohydrate from one receptor molecule binds to protein residues from the dimer-related receptor molecule to form a 'carbohydrate handshake'.

6/7/4

DIALOG(R)File 155:MEDLINE(R)

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09426929 98143739

Antibody against the human J chain inhibits polymeric Ig receptor-mediated biliary and epithelial transport of human polymeric IgA. Vaerman JP; Langendries AE; Giffroy DA; Kaetzel CS; Fiani CM; Moro I; Brandtzaeg P; Kobayashi K

Catholic University of Louvain, Institute of Cell Pathology, Unit of Experimental Medicine, Brussels, Belgium. vaerman@mexp.ucl.ac.be

Eur J Immunol (GERMANY) Jan 1998, 28 (1) p171-82, ISSN 0014-2980
Journal Code: EN5

Languages: ENGLISH

Document type: JOURNAL ARTICLE

To emphasize the requirement for a J chain in native polymeric immunoglobulins for their selective transport into exocrine secretions, IgG, purified from two different antisera specific for the human J chain, was shown to: (i) bind in vitro to human polymeric IgA (pIgA) by density gradient ultracentrifugation; (ii) inhibit binding in vitro of rat secretory component to human pIgA; (iii) inhibit hepatic transport of human pIgA into rat bile in vivo; and (iv) inhibit apical **transcytosis** of pIgA in vitro by polarized human polymeric immunoglobulin receptor (pIgR)-expressing Madin-Darby canine kidney cells. Inhibition of biliary transport increased with the molar ratio of anti-J chain **antibodies** against pIgA and their incubation time. Anti-J chain F(ab')₂ and Fab fragments also inhibited biliary transport, excluding a role for phagocytic clearance or excessive size of the immune complexes. Anti-human-Fc alpha Fab, bound to human pIgA in complexes of larger size than those with anti-J chain Fab, did not inhibit biliary transport of human pIgA. Propionic acid-denatured human pIgA, although containing J chains, was very poorly transported into rat bile. Altogether, our data strongly support, now also by in vivo experiments, the crucial role of the J chain of native pIgA in its selective pIgR-mediated transport into secretions, as suggested long ago by in vitro data only. Recent data on J chain-knockout mice, with low IgA levels in bile and feces, cannot explain the role of the J chain in contributing to the secretory component/pIgR-binding site of normal pIgA, but otherwise agree with our study.

6/7/5

DIALOG(R)File 155:MEDLINE(R)

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09212152 97435422

Image analysis of protein profiles from paired microvillous and basal syncytiotrophoblast plasma membranes from term human placenta and characterization of IgG binding to membrane vesicles.

Eaton BM; Oakey MP

Academic Department of Obstetrics and Gynaecology, Charing Cross and Westminster Medical School, Chelsea and Westminster Hospital, London, UK.

Placenta (ENGLAND) Sep 1997, 18 (7) p569-76, ISSN 0143-4004
Journal Code: PMN

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Image analysis of SDS-PAGE profiles of highly purified, paired maternal-facing (microvillous; MVM) and fetal-facing (basal; BM) plasmalemma membrane vesicles from six term human placentae showed that, while individual MVM or BM profiles were extremely reproducible, the two membrane populations were substantially different--although all of the seven major bands of molecular mass, 98.4, 79.4, 71.1, 45.1, 40.9, 39.5 and 34.5 kDa found in MVM were present, albeit in differing amounts, in BM. BM were characterized by the presence of five low molecular weight bands which were not present in MVM. Despite this consistency of the membrane preparations, binding of ¹²⁵I-IgG or its fragments showed marked variability in both MVM and BM. At pH 7.4, both MVM and BM bound similar amounts of ¹²⁵I-IgG with K_d values of $5.2 \pm 1.9 \times 10^{-6}$ M (s.e., n = 8) and $2.9 \pm 0.4 \times 10^{-6}$ M respectively, (P > 0.05). There were 1.2-1.6 x 10¹⁵ binding sites/mg protein. Affinity constants for Fc fragment binding to MVM and BM were similar to those for IgG, although the B_{max} value for BM Fc binding was greatly reduced compared to that for IgG (P > 0.001). Fab binding to MVM and BM was also saturable but substantially lower than that of Fc, whereas binding of F(ab')₂ was low and linear. Both MVM and BM bound marginally more IgG at pH 6.0 than at pH 7.4. These data provide further evidence for receptor-mediated **transcytosis** of maternal IgG across the placenta and confirm that the placental IgG transporter differs from classical Fc gamma receptors.

6/7/6

DIALOG(R)File 155:MEDLINE(R)

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09059176 97235237

Microvascular permeability to the F(ab')₂ fragment of IgG in the male rat reproductive tract at puberty.

Pollanen P; Cooper TG; Kokk K; Saari T; Setchell BP

Department of Anatomy, University of Turku, Finland. papepo@utu.fi

J Reprod Immunol (IRELAND) Feb 1997, 32 (3) p221-40, ISSN 0165-0378

Journal Code: JWS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Development of contraceptive vaccines has recently raised much interest following the cloning of the sperm and oocyte components involved in the sperm-oocyte interaction. The main difficulty of immunocontraception in the male is the poor access of **antibodies** to the luminal compartment. As recent literature suggests that many substances are transported to the testis by receptor-mediated or fluid-phase **transcytosis**, the dependence of the transport of IgG on the Fc receptor was studied in the present investigation by comparing the penetration of whole IgG and the F(ab')₂ fragment of IgG to the testis and epididymis. The maximum volume of distribution (V_{eq}) for the F(ab')₂ fragment was significantly higher than that for whole IgG in the testis of 30-60-day old rats, in the caput and cauda of 30- and 45-day old rats and the corpus of 45-day old rats. The speeds at which equilibrium between tissue extracellular fluid and serum was reached (K) for the F(ab')₂ fragment and whole IgG were significantly different in the testicular capsule of the 60-day old, in the caput and corpus of the 45- and 60-day old and in the cauda of the 45-day old rats. The microvascular permeabilities (PE) to the F(ab')₂ fragment were more than 2-fold higher than those to whole IgG in the testis of the 20-, 45- and 60-day old, in the testicular capsule of the 20- and 45-day old, in the caput of 20-, 30- and 60-day old and in the corpus of 20-day old rats. The PE to whole IgG was more than 2-fold higher than that to the F(ab')₂ fragment in the cauda of the 45-day-old rats. The PE to the F(ab')₂ fragment increased steadily from 20 to 60 days of age in the testis and caput, but in the corpus there was a more abrupt increase between 30 and 45

days of age. In the cauda, PE remained in the same range of magnitude throughout pubertal development. These results suggest that the F(ab')₂ fragment reaches the lumen of the reproductive tract more easily than whole IgG from 30 days of age onwards in the testis, whereas in the caput, corpus and cauda epididymidis the rate at which F(ab')₂ fragment reaches the lumen increases only temporarily at the time of appearance of spermatozoa in the lumen. Transport of IgG to the male reproductive tract is thus unlikely to be mediated by **Fc** receptors.

6/7/7

DIALOG(R)File 155:MEDLINE(R)

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08829216 96405833

Transcytosis of IgG anti-D by human term trophoblast cells in culture.

Kumpel BM; Sooranna SR

International Blood Group Reference Laboratory, Bristol, U.K.

Transfus Med (ENGLAND) Jun 1996, 6 (2) p115-20, ISSN 0958-7578

Journal Code: BU7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Placental trophoblast cells were cultured on filters that allow access to medium bathing the apical and basal surfaces of cells. Purified human IgG was added to either the apical or the basal chambers and sampled at intervals of up to 100min for determination of IgG concentration by ELISA. Using this experimental system, transport of IgG1 and IgG3 monoclonal anti-D, affinity-purified polyclonal anti-D and human polyclonal IgG were shown to occur primarily in the apical to basal (i.e. maternal to fetal) direction. The overall transport of monoclonal and polyclonal anti-D was less than 10% in 45 min, several times lower than that of IgG. There was no difference in the rate or percentage of transport between IgG1 (BRAD-5) and IgG3 (BRAD-3) monoclonal anti-D. The possibility that the **Fc** receptor mediating **transcytosis** of IgG anti-D through human trophoblast cells in culture is the placental hFcRn is proposed.

6/7/8

DIALOG(R)File 155:MEDLINE(R)

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08671265 96182303

Abnormally short serum half-lives of IgG in beta 2-microglobulin-deficient mice.

Ghetie V; Hubbard JG; Kim JK; Tsen MF; Lee Y; Ward ES

Department of Microbiology, University of Texas Southwestern Medical Center, Dallas 75235-8576, USA.

Eur J Immunol (GERMANY) Mar 1996, 26 (3) p690-6, ISSN 0014-2980

Journal Code: EN5

Contract/Grant No.: AI32413, AI, NIAID; AI33111, AI, NIAID

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The MHC class I-related receptor, **FcRn**, mediates the transfer of maternal gamma globulin (IgG) to young rodents, primarily via intestinal **transcytosis**, and this provides humoral immunity for the first few weeks after birth. In a previous study, the site of mouse IgG1 (mIgG1) with which **FcRn** interacts has been mapped using recombinant wild-type and mutated **Fc** -hinge fragments. The site encompasses residues at the CH2-CH3 domain interface of **Fc** (Ile253, His310, Gln311, His433 and Asn434) and the same amino acids are involved in regulating the

pharmacokinetics of the **Fc**-hinge fragments. This suggests that in addition to its known function, **FcRn** might also play a role in IgG homeostasis. Consistent with this hypothesis, in this study, we demonstrate that **FcRn** alpha-chain mRNA is present not only in neonatal brush border but also in other tissues of adult animals (liver, lung, spleen and endothelial cells). In addition, analysis of the pharmacokinetics of mouse Ig/**Fc**-hinge fragments in genetically manipulated mice that are deficient in the expression of **FcRn** demonstrates that the beta-phase half-lives are abnormally short. These findings suggest that **FcRn** is involved in IgG homeostasis.

6/7/9

DIALOG(R)File 155:MEDLINE(R)

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08075355 95090009

Evidence that **Fc** gamma receptors in rabbit yolk sac endoderm do not depend upon an acid pH to effect IgG binding and **transcytosis** in vitro.

Meads TJ; Wild AE

Department of Biology, School of Biological Sciences, University of Southampton, UK.

Placenta (ENGLAND) Jul 1994, 15 (5) p525-39, ISSN 0143-4004

Journal Code: PMN

Languages: ENGLISH

Document type: JOURNAL ARTICLE

An in vitro culture system has been devised creating apical and basal compartments separated by rabbit visceral yolk sac (VYS) with an intact epithelium. Selective **transcytosis** and binding of heterologous IgG applied to the apical yolk sac endoderm (YSE) was demonstrated in vitro using double label immunofluorescence. Thus, whilst both human and bovine IgG could be detected in endosomes in YSE, only human IgG could be detected in the basement membrane and vascular mesenchyme. This mirrors what is found in vivo. The **Fc** fragment of human Ig was transcytosed but not the Fab fragment, indicating that **Fc** receptors were expressed in the cultured YSE. When VYS was previously chilled to 4 degrees C to prevent endocytosis and treated with rabbit serum albumin to prevent non-specific binding, human IgG, but not bovine IgG, became specifically bound to YSE apical plasma membrane; comparison of binding at pH 6.0, 7.3 (the average pH of rabbit uterine fluid) and 8.0 revealed no obvious difference. Pre-exposure of VYS for up to 5 min in monensin, followed by culture in monensin and immunoglobulin-containing medium, did not prevent the selective transcytosis of human IgG, suggesting that an acidic compartment may not be needed for **transcytosis**. An acid pH dependent **Fc** gamma receptor equivalent to that on suckling rat gut jejunal enterocyte plasma membranes could not be isolated from rabbit YSE following exposure of solubilized membrane to affinity matrix bound IgG at pH 6.0 and elution at pH 8.0. These results contradict a recent suggestion that **Fc** receptors on all IgG transcytosing epithelia require an acid pH to effect IgG binding and selective **transcytosis**.

6/7/10

DIALOG(R)File 155:MEDLINE(R)

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07469401 92034983

Selective inhibition of **transcytosis** by brefeldin A in MDCK cells.

Hunziker W; Whitney JA; Mellman I

Department of Cell Biology, Yale University School of Medicine, New

Haven, Connecticut 06510.

Cell (UNITED STATES) Nov 1 1991, 67 (3) p617-27, ISSN 0092-8674

Journal Code: CQ4

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Treatment of most cells with brefeldin A (BFA) leads to the retrieval of the Golgi complex to the endoplasmic reticulum, presumably reflecting an inhibition of cytoplasmic coat protein binding to Golgi membranes. Although BFA has been thought to act only on biosynthetic organelles, we now show that this drug also reversibly blocks polymeric immunoglobulin receptor-mediated **transcytosis** in MDCK cells. The action of BFA on **transcytosis** was selective, since internalization, recycling, and intracellular degradation were unaffected. The block occurred early on the transcytotic pathway, probably before the translocation of IgA-containing vesicles from the basal to the apical cytoplasm. Although BFA caused MDCK cell endosomes to become more tubular, the organization of the Golgi and binding of the 110 kd Golgi coat protein beta-COP was surprisingly unaffected. These results suggest that in MDCK cells, endocytic organelles contain a BFA-sensitive coat that regulates their organization and function even though the Golgi coat is BFA resistant.

6/7/11

DIALOG(R) File 155:MEDLINE(R)

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05832212 90094532

Expression of macrophage-lymphocyte **Fc** receptors in Madin-Darby canine kidney cells: polarity and **transcytosis** differ for isoforms with or without coated pit localization domains.

Hunziker W; Mellman I

Department of Cell Biology, Yale University School of Medicine, New Haven, Connecticut 06510.

J Cell Biol (UNITED STATES) Dec 1989, 109 (6 Pt 2) p3291-302, ISSN 0021-9525 Journal Code: HMV

Contract/Grant No.: CA-46128, CA, NCI; GM-29765, GM, NIGMS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Many cells of the immune system and certain epithelia express receptors for the **Fc** domain of IgG (**FcR**). On mouse macrophages and lymphocytes, two distinct receptor isoforms have been identified, designated **FCRII-B1** and **FCRII-B2**. The isoforms are identical except for an in-frame insertion of 47 amino acids in the cytoplasmic tail of **FCRII-B1** that blocks its ability to be internalized by clathrin-coated pits. We have recently found that at least one IgG-transporting epithelium, namely placental syncytial trophoblasts, expresses transcripts encoding a receptor similar or identical to macrophage-lymphocyte **FCRII**. To determine whether **FCRII** of hematopoietic cells might also function as a transcytotic receptor if expressed in epithelial cells, **FCRII-B1** and **-B2** were transfected into Madin-Darby canine kidney (MDCK) cells and grown on permeable filter units. The two **FCRII** isoforms exhibited different patterns of polarized expression: **FCRII-B1** was localized mainly to the apical plasma membrane domain, whereas **FCRII-B2** was found predominantly on the basolateral surface. As expected for **FcR** in placenta, **FCRII-B2** and to a lesser extent **FCRII-B1** mediated transcellular transport of IgG-complexes from the apical to the basolateral plasma membrane. Neither receptor mediated **transcytosis** in the opposite direction, although **FCRII-B2** also delivered ligand to lysosomes when internalized from either the basolateral or apical domains. Furthermore, **FCRII-B2** was capable of transporting monovalent antireceptor antibody Fab

fragments across the cell, suggesting that **transcytosis** was not dependent on receptor cross-linking. These findings suggest the possibility that **FcRII** can mediate transepithelial IgG transport when expressed in placental syncytial trophoblasts in addition to its "classical" endocytic and signaling activities when expressed in macrophages. Because **FcRII** -B1 and -B2 are expressed with distinct polarities, the results also suggest that interactions with clathrin-coated pits may play a role in generating the polarized distribution of at least some plasma membrane proteins in MDCK cells.
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